



10

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Garcia-Blanco, Mariano A.
Walsh, Christopher E.
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<120> METHODS AND COMPOSITIONS FOR USE IN
SPLICEOSOME MEDIATED RNA TRANS-SPLICING

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<140> 09/838,858
<141> 2001-04-20

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<150> 09/756,096
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38

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<220>
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37

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<400> 34

ctgactgcag ggtaaccgga caaggacact gcttcacc

38

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<400> 35

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35

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<211> 37

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<213> Artificial Sequence

<220>

<223> Oligonucleotide primer

<400> 36

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<400> 46
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<400> 48
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<400> 52
aactagaagg cacagtcgag g 21

<210> 53
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<220>
<223> Trans-spliced product containing humanchorionic
gonadotropin gene 6 sequences and Corynebacterium
diphtheriae toxin A sequence

<400> 53
gagatgttcc agggcgtgat gatg 24

<210> 54
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<223> A, C, G or U

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<222> (57)...(70)
<223> Loop comprising a combination of 14 nucleotides

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nnnnnnnnnn aucguuaacu aaauaacuac uaacuggggug aacuucuguu uuuuucucga 120
gcugcag 127

<210> 55
<211> 127

<212> RNA
<213> Artificial Sequence

<220>
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<221> unsure
<222> (57)...(70)
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nnnnnnnnnn aucguuaacu aaauaacuac uaacuggggug aacuucugua uuauucucga 120
gcugcag 127

<210> 56
<211> 127
<212> RNA
<213> Artificial Sequence

<220>
<223> PTM intramolecular base paired stem

<221> unsure
<222> (57)...(70)
<223> A, C, G or U

<221> misc_feature
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<223> Loop comprising a combination of 14 nucleotides

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gcugcag 127

<210> 57
<211> 132
<212> DNA
<213> Artificial Sequence

<220>
<223> Trans-spliced product containing human chorionic gonadotropin gene 6 sequences and Corynebacterium diptheriae diptheria toxin A sequences

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tccattcaaa aa 132

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<223> Artificial Sequence derived from Escherichia coli
lacZ gene

<400> 58
gaattcggta ccatgggg 18

<210> 59
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lacZ gene

<400> 59
cgtttacagg taagaggatc ctccggaggg ccc 33

<210> 60
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<220>
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lacZ gene

<400> 60
tggtgtcaaa aataataagt taacaagctt 30

<210> 61
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<220>
<223> Trans-spliced product containing Escherichia coli
lacZ gene sequences and human chorionic
gonadotropin gene 6 exon 2 sequences

<400> 61
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25

<210> 62
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<212> DNA
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<220>
<223> Trans-spliced product containing Escherichia coli
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acgggcaacc cgtggtcggc ttacggcggg gattttggcg atacgccgaa cgatcgccag 240
ttctgtatga acggtctggt ctttgccgac cgcacgccgc atccag 286

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<220>
<223> Trans-spliced product containing Escherichia coli
lacZ gene sequences

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ttcggccacg gtgccg 196

<210> 64
<211> 420
<212> DNA
<213> Artificial Sequence

<220>
<223> Trans-spliced product containing cystic fibrosis
transmembrane regulator-derived sequences and
His-tag sequence

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tgatgattat gggagaactg gaggcttcag agggtaaaat taagcacagt ggaagaattt 180
cattctgttc tcagttttcc tggattatgc ctggcaccat taaagaaaat atcatctttg 240

gcggccgcca ctgtgctgga tatctgcaga attccaccac actggactag tggatccgag 300
ctcggtacca aggttaagtt taaaccgctg atcagcctcg actgtgcctt ctagttgcca 360
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<212> DNA

<213> Artificial Sequence

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<223> Splice junction sequence

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<210> 66

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> C terminal residus from glutathione-S- tranferase

<400> 66

Asp Tyr Lys Asp Asp Lys

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<210> 67

<211> 15

<212> DNA

<213> Artificial Sequence

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<223> Artificial sequence comprising sequences derived
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<400> 67

ggagttgatc ccgtc

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<210> 68

<211> 37

<212> DNA

<213> Artificial Sequence

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<223> Artificial sequence comprising sequences derived
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<210> 69
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<223> Binding domain of PTM

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<220>
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<400> 70
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<223> Branch point, pyrimidine tract and acceptor splice
site of PTM

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47

<210> 72
<211> 70
<212> DNA
<213> Artificial Sequence

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<223> Donor site and spacer sequence of PTM

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gatccaccgg 70

<210> 73
<211> 260
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<213> Artificial Sequence

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<223> Binding domain of spacer sequence

<400> 73
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ctggaaaact gataacacaa tgaaattctt ccactgtgct taaaaaaacc ctcttgaatt 180
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aactcattat caaatcacgc 260

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<210> 75
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actcagtgtg attccacctt ctc 23

<210> 76
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gacctctgca gacttcactt ctaatgatga ttatgg 36

<210> 77

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ctaggatccc gttcttttgt tcttcactat taa

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<210> 78
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<400> 78
ctagggttac cgaagtaaaa ccatacttat tag

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<210> 79
<211> 35
<212> DNA
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<220>
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<400> 79
gcatgggttac cctgcagggg ctgctgctgt tgctg

35

<210> 80
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer

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ctgaaagctt gttaaccagc tcaccatggt ggggcag

37

<210> 81
<211> 23
<212> DNA
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<220>
<223> Binding domain of PTM molecule

<400> 81
acccatcatt attaggtcat tat

23

<210> 82
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer

<400> 82
gatcaaattct gtcgatacctt cc

22

<210> 83
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer

<400> 83
ctgatccacc cagtcccatt a

21

<210> 84
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide primer

<400> 84
gactgatcca cccagtcca ga

22

<210> 85
<211> 52
<212> DNA
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site.

<221> misc_feature
<222> (7)...(30)
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<221> unsure
<222> (7)...(30)
<223> A, C, G or T

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<211> 71
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

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tatgatgaaa a 71

<210> 87
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 87
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acgccg 66

<210> 88
<211> 192
<212> DNA
<213> Artificial Sequence

<220>
<223> PTM sequence

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tccggccgca tcagcttttg cagccaattc agttggatca tgcccggtac catcaaggag 120
aacataatct tcggcgtcag ttacgacgag taccgctatc gctcggtgat taaggcctgt 180
cagttggagg ag 192

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<212> DNA
<213> Artificial Sequence

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<223> Oligonucleotide

<400> 89

gagcaggcaa gacgagcttg ctcat

25

<210> 90

<211> 28

<212> DNA

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<223> Oligonucleotide

<400> 90

gagaacataa tcttcggcgt cagttacg

28

<210> 91

<211> 30

<212> DNA

<213> Artificial Sequence

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<223> Oligonucleotide

<400> 91

gtcagttgga ggaggacatc tccaagtttg

30

<210> 92

<211> 192

<212> DNA

<213> Artificial Sequence

<220>

<223> Oligonucleotide

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aacataatct tcggcgtcag ttacgacgag taccgctatc gtcggtgat taaggcctgt 180
cagttggagg ag 192

<210> 93

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> PTM sequences

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aaatatcatt ggtgttttctt atgatga

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<210> 94
<211> 30
<212> DNA
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<220>
<223> Oligonucleotide

<400> 94
ccaactagaa gaggacatct ccaagtttgc

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<210> 95
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<212> DNA
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<220>
<223> Oligonucleotide

<400> 95
atgatcatgg gcgagttaga accaagtgag

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<210> 96
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<212> DNA
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<220>
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<400> 96
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27

<210> 97
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Oligonucleotide

<400> 97
ccaactagaa gaggacatct ccaagtt

27

<210> 98
<211> 21
<212> DNA

<213> Artificial Sequence

<220>

<223> 5' splice site

<400> (98

cgtttacagg taagtggatc c

21

<210> 99

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> 3' splice site

<400> 99

ctgcagggcg gcttcgtcta ataatgg

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<210> 100

<211> 65

<212> DNA

<213> Artificial Sequence

<220>

<223> Sequence from trans-splicing domain

<221> unsure

<222> (7)...(18)

<223> A, C, G or T

<400> 100

gctagcnnnc cgcggnnnta ctaactggta cctcttcttt tttttttgat atcctgcagg 60
gcggc 65

<210> 101

<211> 1584

<212> DNA

<213> Artificial Sequence

<220>

<223> CFTR PTM

<400> 101

atgcagaggt cgcctctgga aaaggccagc gttgtctcca aacttttttt cagctggacc 60
agaccaattt tgaggaaagg atacagacag cgcctggaat tgtcagacat ataccaaatc 120
ccttctgttg attctgctga caatctatct gaaaaatttg aaagagaatg ggatagagag 180
ctggcttcaa agaaaaatcc taaactcatt aatgcccttc ggcgatgttt tttctggaga 240
tttatgttct atggaatctt tttatattta ggggaagtca ccaaagcagt acagcctctc 300
ttactgggaa gaatcatagc ttcctatgac ccggataaca aggaggaacg ctctatcgcg 360

atttatctag gcataggctt atgccttctc tttattgtga ggacactgct cctacaccca 420
 gccatttttg gccttcatca cattggaatg cagatgagaa tagctatgtt tagtttgatt 480
 tataagaaga ctttaaagct gtcaagccgt gttctagata aaataagtat tggacaactt 540
 gttagtctcc ttccaacaa cctgaacaaa tttgatgaag gacttgcatt ggcacatttc 600
 gtgtggatcg ctcccttgca agtggcactc ctcatggggc taatctggga gttgttacag 660
 gcgtctgcct tctgtggact tggtttctg atagtccttg ccttttttca ggctgggcta 720
 gggagaatga tgatgaagta cagagatcag agagctggga agatcagtga aagacttggtg 780
 attacctcag aaatgatcga gaacatccaa tctgttaagg catactgctg ggaagaagca 840
 atggaaaaaa tgattgaaaa cttaagacaa acagaactga aactgactcg gaaggcagcc 900
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 tgggaggagg gatttgggga attatttgag aaagcaaaac aaaacaataa caatagaaaa 1260
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 ctgaaagata ttaatttcaa gatagaaaga ggacagttgt tggcggttgc tggatccact 1380
 ggagcaggca agacgagctt gctcatgatg atcatgggcg agttagaacc aagtgaaggc 1440
 aagatcaaac attccggccg catcagcttt tgcagccaat tcagttggat catgcccggt 1500
 accatcaagg agaacataat cttcggcgtc agttacgacg agtaccgcta tcgctcggtg 1560
 attaaggcct gtcagttgga ggag 1584

<210> 102

<211> 323

<212> DNA

<213> Artificial Sequence

<220>

<223> Trans-splicing domain of CFTR PTM

<400> 102

gtaagatate accgatatgt gtctaacctg attcgggcct tcgatacgct aagatccacc 60
 ggtcaaaaag ttttcacata atttcttacc tcttcttgaa ttcatgcttt gatgacgctt 120
 ctgtatctat attcatcatt ggaacaccca atgatatttt cttaaatggt gcctggcata 180
 atcctggaaa actgataaca caatgaaatt cttccactgt gcttaatttt accctctgaa 240
 ttctccattt ctcccataat catcattaca actgaactct ggaaataaaa cccatcatta 300
 ttaactcatt atcaaatcac gct 323

<210> 103

<211> 165

<212> DNA

<213> Artificial Sequence

<220>

<223> PTM binding domain

<400> 103

gctagcaata atgacgaagc cgccctcac gctcaggatt cacttgccct caattatcat 60
 cctaagcaga agtgtatatt cttatttgta aagattctat taactcattt gattcaaaa 120
 atttaaaata ctctctgttt cacctactct gctatgcacc cgcg 165

<210> 104
 <211> 225
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Trans-splicing domain of PTM

<400> 104
 aataatgacg aagccgcccc tcacgctcag gattcacttg cctccaatt atcatcctaa 60
 gcagaagtgt atattcttat ttgtaaagat tctattaact catttgattc aaaatattta 120
 aaatacttcc tgtttcacct actctgctat gcaccgcgg aacattatta taacgttgct 180
 cgaatactaa ctggtacctc ttcttttttt ttgatatcc tgcag 225

<210> 105
 <211> 3069
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> CFTR PTM sequence

<400> 105
 acttcacttc taatgatgat tatgggagaa ctggagcctt cagagggtaa aattaagcac 60
 agtggaagaa tttcattctg ttctcagttt tcctggatta tgccctggcac cattaaagaa 120
 aatatcatct ttggtgtttc ctatgatgaa tatagataca gaagcgtcat caaagcatgc 180
 caactagaag aggacatctc caagtttgca gagaaagaca atatagttct tggagaaggt 240
 ggaatcacac tgagtggagg tcaacgagca agaatttctt tagcaagagc agtatacaaa 300
 gatgctgatt tgtatttatt agactctcct tttggatacc tagatgtttt aacagaaaaa 360
 gaaatatttg aaagctgtgt ctgtaaactg atggctaaca aaactaggat tttggtcact 420
 tctaaaatgg aacattttaa gaaagctgac aaaatattaa ttttgcatga aggttagcagc 480
 tatttttatg ggacattttc agaactccaa aatctacagc cagacttttag ctcaaaactc 540
 atgggatgtg attcttttcga ccaatttagt gcagaaagaa gaaattcaat cctaactgag 600
 accttacacc gtttctcatt agaaggagat gctcctgtct cctggacaga aacaaaaaaa 660
 caatctttta aacagactgg agagtgtggg gaaaaaagga agaattctat tctcaatcca 720
 atcaactcta tacgaaaatt ttccattgtg caaaagactc ccttacaat gaatggcatc 780
 gaagaggatt ctgatgagcc tttagagaga aggctgtcct tagtaccaga ttctgagcag 840
 ggagaggcga tactgcctcg catcagcgtg atcagcactg gccccacgct tcaggcacga 900
 aggaggcagt ctgtcctgaa cctgatgaca cactcagtta accaagggtca gaacattcac 960
 cgaaagacaa cagcatccac acgaaaagtg tcaactggccc cttaggcaaa cttgactgaa 1020
 ctggatatat attcaagaag gttatctcaa gaaactggct tggaaataag tgaagaaatt 1080
 aacgaagaag acttaaagga gtgctttttt gatgatatgg agagcatacc agcagtgact 1140
 acatggaaca cataccttcg atatattact gtccacaaga gcttaatttt tgtgctaatt 1200
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 actttgcttg ctatgggatt cttcagaggt ctaccactgg tgcatactct aatcacagt 1440
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 aacacgttga aagcaggtgg gattcttaat agattctcca aagatatagc aatttttgat 1560

gaccttctgc	ctcttaccat	atttgacttc	atccagttgt	tattaattgt	gattggagct	1620
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gcttttatta	tggtgagagc	atatttcctc	caaaccctac	agcaactcaa	acaactggaa	1740
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cttcgtgcct	tcggacggca	gccttacttt	gaaactctgt	tccacaaagc	tctgaattta	1860
catactgcc	actggttctt	gtacctgtca	acactgcgct	ggttccaa	gagaatagaa	1920
atgatttttg	tcattcttctt	cattgctgtt	accttcattt	ccattttaac	aacaggagaa	1980
ggagaaggaa	gagttggtat	tatcctgact	ttagccatga	atatcatgag	tacattgcag	2040
tggtgctgt	actccagcat	agatgtggat	agcttgatgc	gatctgtgag	ccgagtcttt	2100
aagttcattg	acatgccaac	agaaggtaaa	cctaccaagt	caaccaaacc	atacaagaat	2160
ggccaactct	cgaaagttat	gattattgag	aattcacacg	tgaagaaaga	tgacatctgg	2220
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gccatattag	agaacatttc	cttctcaata	agtcctggcc	agagggtggg	cctcttggga	2340
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ggagaaatcc	agatcgatgg	tgtgtcttgg	gattcaataa	ctttgcaaca	gtggaggaaa	2460
gcctttggag	tgataccaca	gaaagtattt	attttttctg	gaacatttag	aaaaaacttg	2520
gatccctatg	aacagtggag	tgatcaagaa	atatggaaag	ttgcagatga	ggttgggctc	2580
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gtcctaagcc	atggccacaa	gcagttgatg	tgcttggcta	gatctgttct	cagtaaggcg	2700
aagatcttgc	tgcttgatga	accagtgct	catttggatc	cagtaacata	ccaaataatt	2760
agaagaactc	taaaacaagc	atttgcctgat	tgcacagtaa	ttctctgtga	acacaggata	2820
gaagcaatgc	tggaatgcca	acaatttttg	gtcatagaag	agaacaaagt	gcggcagtag	2880
gattccatcc	agaaactgct	gaacgagagg	agcctcttcc	ggcaagccat	cagcccctcc	2940
gacaggggtga	agctctttcc	ccaccggaac	tcaagcaagt	gcaagtctaa	gccccagatt	3000
gctgctctga	aagaggagac	agaagaagag	gtgcaagata	caaggcttca	tcattcatcat	3060
catcattag						3069

<210> 106

<211> 131

<212> DNA

<213> Artificial Sequence

<220>

<223> Binding domain of mouse factor VIII PTM

<400> 106

ctcgagctta	cctgaactaa	tttttttagaa	tattaaaatc	ctaagctttt	atatctctat	60
ccctctatct	tttgctctct	atccaatttt	tattaactta	gacttttaaa	agaaacttat	120
gagaaaaatt	t					131

<210> 107

<211> 71

<212> DNA

<213> Artificial Sequence

<220>

<223> Spacer sequence of PTM

<400> 107

ccgcggaaca	ttattataac	gttgctcgaa	tactaactgg	tacctcttct	tttttttttg	60
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atatcctgca g

71

<210> 108

<211> 527

<212> DNA

<213> Artificial Sequence

<220>

<223> Chicken beta actin promoter sequences

<400> 108

```
ccatggtcga cgtagcccc acgtttctgct tcaactctccc catctccccc ccctccccac 60
ccccaatttt gtatttattt attttttaat tattttgtgc agcgatgggg gcgggggggg 120
ggggggggcg cgcgccaggc ggggcggggc ggggcgaggg gcggggcggg gcgagggcga 180
gaggtgcggc ggcagccaat cagagcggcg cgctccgaaa gttcctttta tcgcgagggc 240
gcggcgggcg cggccctata aaaagcgaag cgcgcggcgg ccgggagtcg ctgcgacgct 300
gccttcgccc cgtgcccaacc tccgcctcga gcttacctga actaattttt tagaatatta 360
aaatcctaag cttttatact cctatccctc tatcttttgc tctctatcca atttttatta 420
acttagactt taaaaagaaa cttatgagaa aaatttccgc ggaacattat tataacgttg 480
ctcgaatact aactggtacc tcttcttttt tttttgatat cctgcag 527
```

<210> 109

<211> 169

<212> DNA

<213> Artificial Sequence

<220>

<223> Sequence not included in construct

<400> 109

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cgccgcctcg cgccgcccgc cccggtcttg actgaccgcg ttactcccac aggtgagcgg 60
gcgggacggc ccttctcctc cgggctgtaa ttagcgcttg gtttaatcac ggcttgtttc 120
ttttctgtgg ctgcgtgaaa gccttgaggg gctccgggag gaattcgta 169
```

<210> 110

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> F8 PTM sequences

<400> 110

```
ggagtcgctg cgacgctgcc ttcgccccgt gccaacctcc gc 42
```

<210> 111

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> F8 PTM sequences

<400> 111

ctcgagcacc gatatcgtaa ct

22

<210> 112

<211> 53

<212> DNA

<213> Artificial Sequence

<220>

<223> Exon 26, Flag tag, stop sequences of mouse factor
VIII PTM

<400> 112

gagggccagc agcaatacga ctacaaggac gacgatgaca agtgagttta aac

53

<210> 113

<211> 71

<212> DNA

<213> Artificial Sequence

<220>

<223> Spacer sequences of human or canine factor VIII
PTM

<400> 113

ccgcggaaca ttattataac gttgctcgaa tactaactgg tacctcttct tttttttttg 60
atatcctgca g 71